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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/620,091	07/15/2003	Steve Roffler	4910-2DIV2	8710

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EXAMINER

FETTEROLF, BRANDON J

ART UNIT	PAPER NUMBER
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1642

DATE MAILED: 08/16/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

<b>Advisory Action</b> <b>Before the Filing of an Appeal Brief</b>	<b>Application No.</b> 10/620,091	<b>Applicant(s)</b> ROFFLER ET AL.	
	<b>Examiner</b> Brandon J. Fetterolf, PhD	<b>Art Unit</b> 1642	

**--The MAILING DATE of this communication appears on the cover sheet with the correspondence address --**

THE REPLY FILED 28 July 2006 FAILS TO PLACE THIS APPLICATION IN CONDITION FOR ALLOWANCE.

1. ☒ The reply was filed after a final rejection, but prior to or on the same day as filing a Notice of Appeal. To avoid abandonment of this application, applicant must timely file one of the following replies: (1) an amendment, affidavit, or other evidence, which places the application in condition for allowance; (2) a Notice of Appeal (with appeal fee) in compliance with 37 CFR 41.31; or (3) a Request for Continued Examination (RCE) in compliance with 37 CFR 1.114. The reply must be filed within one of the following time periods:

- a) ☐ The period for reply expires \_\_\_\_\_ months from the mailing date of the final rejection.  
 b) ☒ The period for reply expires on: (1) the mailing date of this Advisory Action, or (2) the date set forth in the final rejection, whichever is later. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of the final rejection.

Examiner Note: If box 1 is checked, check either box (a) or (b). ONLY CHECK BOX (b) WHEN THE FIRST REPLY WAS FILED WITHIN TWO MONTHS OF THE FINAL REJECTION. See MPEP 706.07(f).

Extensions of time may be obtained under 37 CFR 1.136(a). The date on which the petition under 37 CFR 1.136(a) and the appropriate extension fee have been filed is the date for purposes of determining the period of extension and the corresponding amount of the fee. The appropriate extension fee under 37 CFR 1.17(a) is calculated from: (1) the expiration date of the shortened statutory period for reply originally set in the final Office action; or (2) as set forth in (b) above, if checked. Any reply received by the Office later than three months after the mailing date of the final rejection, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

#### NOTICE OF APPEAL

2. ☐ The Notice of Appeal was filed on \_\_\_\_\_. A brief in compliance with 37 CFR 41.37 must be filed within two months of the date of filing the Notice of Appeal (37 CFR 41.37(a)), or any extension thereof (37 CFR 41.37(e)), to avoid dismissal of the appeal. Since a Notice of Appeal has been filed, any reply must be filed within the time period set forth in 37 CFR 41.37(a).

#### AMENDMENTS

3. ☒ The proposed amendment(s) filed after a final rejection, but prior to the date of filing a brief, will not be entered because  
 (a) ☒ They raise new issues that would require further consideration and/or search (see NOTE below);  
 (b) ☐ They raise the issue of new matter (see NOTE below);  
 (c) ☐ They are not deemed to place the application in better form for appeal by materially reducing or simplifying the issues for appeal; and/or  
 (d) ☐ They present additional claims without canceling a corresponding number of finally rejected claims.

NOTE: \_\_\_\_\_. (See 37 CFR 1.116 and 41.33(a)).

4. ☐ The amendments are not in compliance with 37 CFR 1.121. See attached Notice of Non-Compliant Amendment (PTOL-324).  
 5. ☐ Applicant's reply has overcome the following rejection(s): \_\_\_\_\_.  
 6. ☐ Newly proposed or amended claim(s) \_\_\_\_\_ would be allowable if submitted in a separate, timely filed amendment canceling the non-allowable claim(s).  
 7. ☒ For purposes of appeal, the proposed amendment(s): a) ☒ will not be entered, or b) ☐ will be entered and an explanation of how the new or amended claims would be rejected is provided below or appended.  
 The status of the claim(s) is (or will be) as follows:  
 Claim(s) allowed: \_\_\_\_\_.  
 Claim(s) objected to: \_\_\_\_\_.  
 Claim(s) rejected: 21-25, 27-33 and 35-39.  
 Claim(s) withdrawn from consideration: \_\_\_\_\_.

#### AFFIDAVIT OR OTHER EVIDENCE

8. ☐ The affidavit or other evidence filed after a final action, but before or on the date of filing a Notice of Appeal will not be entered because applicant failed to provide a showing of good and sufficient reasons why the affidavit or other evidence is necessary and was not earlier presented. See 37 CFR 1.116(e).  
 9. ☐ The affidavit or other evidence filed after the date of filing a Notice of Appeal, but prior to the date of filing a brief, will not be entered because the affidavit or other evidence failed to overcome all rejections under appeal and/or appellant fails to provide a showing of good and sufficient reasons why it is necessary and was not earlier presented. See 37 CFR 41.33(d)(1).  
 10. ☐ The affidavit or other evidence is entered. An explanation of the status of the claims after entry is below or attached.

#### REQUEST FOR RECONSIDERATION/OTHER

11. ☐ The request for reconsideration has been considered but does NOT place the application in condition for allowance because: \_\_\_\_\_.  
 12. ☐ Note the attached Information Disclosure Statement(s). (PTO/SB/08 or PTO-1449) Paper No(s). \_\_\_\_\_.  
 13. ☐ Other: \_\_\_\_\_.

***Response to the Amendment***

The Amendment filed on 07/28/2006 in response to the previous Final Office Action (3/24/2006) is acknowledged, but has not been entered. The amendment has not been entered because it would involve a new search of the prior art with respect to an antibody produced against a RH1- $\beta$ G-PEG conjugate, as well as, possibly raise new rejections with respect to 112 2<sup>nd</sup> paragraph, omission of essential steps.

Therefore, claims 21-25, 27-33 and 35-39 are currently pending and under consideration.

**The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office Action.**

**Objections Maintained:**

***Specification***

The specification is objected to as failing to provide proper antecedent basis for the claimed subject matter in claims 38 and 39. See 37 CFR 1.75(d)(1) and MPEP § 608.01(o). Correction of the following is required:

For each deposit made pursuant to the regulations for Deposit of Biological Material set forth in MPEP 1801, the specification shall contain:

- (1) The accession number for the deposit;
- (2) The date of the deposit;
- (3) A description of the deposited biological material sufficient to specifically identify it and to permit examination; and
- (4) The name and address of the depository.

**Rejections Maintained:**

***Claim Rejections - 35 USC § 112***

The following is a quotation of the first paragraph of 35 U.S.C. 112:

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The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 21-25, 27-33 and 35-39 remain rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. In the instant case, the claims are inclusive of a genus of polyethylene glycol-containing compounds, which are cleared by an anti-polyethylene glycol antibody, and a genus of polyethylene glycol-containing conjugates comprising a tumor targeting means and a means for activating a genus of anti-tumor prodrug used for treating a tumor. However, the written description in this case only sets forth a polyethylene glycol-containing compound consisting of a PEG-modified  $\beta$ G which may be further covalently linked to a F(ab')<sub>2</sub> fragment of mAb B72.3 or mAb H25 and one species of polyethylene glycol-conjugates used for the treatment of a tumor, wherein the tumor targeting "agent" is a F(ab')<sub>2</sub> fragment of mAb B72.3 covalently linked to a PEG-modified  $\beta$ G which activates one species of prodrug referred to as the tetra n-butyl ammonium salt of glucuranoid derivative of p-hydroxyaniline mustard.

The specification teaches (page 8, lines 11-13) that specific polyethylene glycol-containing compounds of the invention include, but are not limited to, compounds which are cleared from the circulation by an antibody against PEG with out significant toxic side effects. The specification further teaches (page 8, lines 9-11 and page 9, lines 7-9) the development of PEG-modified compounds which are useful in cancer therapy, wherein the PEG-containing compound comprises a tumor targeting means and a means for activating an anti-tumor prodrug to the patient. Although the specification (page 19) discloses the accelerated clearance of two polyethylene glycol containing compounds comprising a PEG-modified  $\beta$ G covalently linked to mAb's B72.3 or H25, the written description (page 43, lines 3+) only appears to reasonably convey one species polyethylene glycol-conjugates used for the treatment of a tumor, wherein the tumor targeting "agent" is a F(ab')<sub>2</sub> fragment of mAb B72.3 covalently linked to a PEG-modified  $\beta$ G which activates one species of prodrug referred to as the tetra n-butyl ammonium salt of a glucuranoid derivative of p-hydroxyaniline mustard. A description of a genus may be achieved by means of a recitation of a

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representative number of species falling within the scope of the genus or by describing structural features common the genus that “constitute a substantial portion of the genus.” See University of California v. Eli Lilly and Co., 119 F.3d 1559, 1568, 43 USPQ2d 1398, 1406 (Fed. Cir. 1997): “A description of a genus of cDNAs may be achieved by means of a recitation of a representative number of cNDA, defined by nucleotide sequence, falling within the scope of the genus or of a recitation of structural features common to the members of the genus, which features constitute a substantial portion of the genus.”

The court has since clarified that this standard applies to compounds other than cDNAs. See University of Rochester v. G.D. Searle & Co., Inc., \_\_\_ F.3d \_\_\_, 2004 WL 260813, at \*9 (Fed.Cir.Feb. 13, 2004). The instant specification fails to provide sufficient descriptive information, such as definitive structural or functional features that are common to the genus. That is, the specification provides neither a representative number of compounds that encompass the genus of polyethylene glycol-containing compound which are rapidly cleared from blood circulation by administration of an anti-polyethylene glycol antibody nor does it provide a description of structural features that are common to the compounds. Further, the specification fails to provide a representative number of conjugates that encompass the genus of polyethylene glycol-containing conjugates comprising a tumor targeting means and a means for activating a genus of anti-tumor prodrug used for treating a tumor nor does it provide a description of structural features that are common to the conjugates. Since the disclosure fails to describe the common attributes or characteristics that identify members of the genus, and because the genus is highly variant, the disclosure of two species of polyethylene glycol-containing compounds, which are cleared by an anti-polyethylene glycol antibody and one species of polyethylene glycol-containing conjugates comprising one tumor targeting means and one means for activating a single anti-tumor prodrug used for treating a tumor is insufficient to describe the genus. Thus, one of skill in the art would reasonably conclude that the disclosure fails to provide a representative number of species to describe and enable the genus as broadly claimed.

*Vas-Cath Inc. v. Mahurkar*, 19USPQ2d 1111, clearly states “applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of the invention. The invention is, for purposes of the ‘written description’ inquiry, *whatever is now claimed*.” (See page 1117.) The specification does not “clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed.” (See *Vas-Cath* at page 1116). As

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discussed above, the skilled artisan cannot envision the detailed chemical structure(s) of the encompassed genus of polyethylene-glycol containing compounds and conjugates, and therefore conception is not achieved until reduction to practice has occurred, regardless of the complexity or simplicity of the method of isolation. Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method of isolating it. The compound itself is required. See *Fiers v. Revel*, 25 USPQ2d 1601 at 1606 (CAFC 1993) and *Amgen Inc. v. Chugai Pharmaceutical Co. Ltd.*, 18 USPQ2d 1016.

One cannot describe what one has not conceived. See *Fiddes v. Baird*, 30 USPQ2d 1481 at 1483. In *Fiddes*, claims directed to mammalian FGF's were found to be unpatentable due to lack of written description for that broad class. The specification provided only the bovine sequence.

Therefore, only two species of polyethylene glycol-containing compound consisting of a PEG-modified  $\beta$ G which may be further covalently linked to a F(ab')<sub>2</sub> fragment of mAb B72.3 or mAb H25 and one species of polyethylene glycol-conjugates used for the treatment of a tumor, wherein the tumor targeting "agent" is a F(ab')<sub>2</sub> fragment of mAb B72.3 covalently linked to a PEG-modified  $\beta$ G which activates one species of prodrug referred to as the tetra n-butyl ammonium salt of glucuranoid derivative of p-hydroxyaniline mustard, but not the full breadth of the claims, meets the written description provision of 35 U.S.C. §112, first paragraph. Applicant is reminded that *Var-Cath* makes clear that the written description provision of 35 U.S.C. §112 is severable from its enablement provision (see page 1115).

In response to this rejection, Applicants contend that claims 21-29 have been amended to recite that the compounds are limited to those capable of binding to an anti-polyethylene glycol monoclonal antibody that is produced by immunizing a mouse with a RH1- $\beta$ G-PEG conjugate, and that the anti-polyethylene glycol monoclonal antibody is limited to that which is produced by immunizing a mouse with a RH1- $\beta$ G-PEG conjugate.

These arguments have been carefully considered, but because Applicant's arguments appear to be solely drawn to the non-elected subject matter, such arguments have not been considered.

Therefore, NO claim is allowed

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Any inquiry concerning this communication or earlier communications from the examiner should be directed to Brandon J. Fetterolf, PhD whose telephone number is (571)-272-2919. The examiner can normally be reached on Monday through Friday from 7:30 to 4:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jeff Siew can be reached on 571-272-0787. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

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Art Unit 1642

  
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BF